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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,116	11/20/2001	John H. Healey	850-PCT-US	6037

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EXAMINER	
JAGOE, DONNA A	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
01/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/890,116	HEALEY ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *77,89-92 and 117* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *77,89-92 and 117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 5, 2007 has been entered.

Claims 77, 89-92 and 117 are pending in this application.

Applicants' arguments filed November 9, 2007 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 77, 89-92 and 117 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 77 recites the composition wherein the bone-cement is molymethylacrylate and the anti-resorptive agent is pamidronate or etidronate or a salt thereon and the bone cement comprises **about 1% or more** by weight of the anti-resorptive agent. With respect to changing numerical range limitations, the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure. In the decision in *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976), the ranges described in the original specification included a range of "25%-60%" and specific examples of "36%" and "50%." A corresponding new claim limitation to "**at least 35%**" did not meet the description requirement because the phrase "at least" had **no upper limit** and caused the claim to read literally on embodiments outside the "25% to 60%" range, however a limitation to "between 35% and 60%" did meet the description requirement. In the instant case, the specification teaches that the antiresorptive agent to be mixed is from about 1 µg to about 11 grams per 60 grams of bone cement dough. The recitation of about 1% or more causes the claim to read on an amount of

antiresorptive agent that is outside the limitations of the recited 1µg to about 11 grams per 60 grams of bone dement dough.

Claims 89-92 and 117 are indefinite to the extent that they read on the rejected base claims in that they do not contain an upper limit for the amount of anti-resorptive agent..

Claim Rejections - 35 USC § 102/103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 77, 89-92 and 117 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Merck & Co. WO 96/39107 and Sabokbar et al. and in further view of Remington's Pharmaceutical Sciences, 15th Edition, 1975, pages 1569-1570.

The claims are drawn to a composition comprising a monomeric bone cement component and a polymeric bone cement component and an anti-resorptive agent component to prevent loosening of the polymerized bone cement matrix from a living bone to which it is attached.

Sabokbar et al. teach a polymethylmethacrylate (PMMA) bone cement, mixed with the bisphosphonate, etidronate, to inhibit bone resorption (see abstract). Specifically, PMMA was mixed with crushed etidronate and then polymerized according to manufacturer's instructions (see Methods). The extent of resorption was significantly

less in the PMMA with etidronate than in PMMA alone suggesting that incorporation of a bisphosphonate into bone cement to inhibit macrophage-osteoclast differentiation may effectively be used to control periprosthetic osteolysis (see discussion). Sabokbar et al. teach that bisphosphonates, included in bone cement may be used to prevent or to control the bone resorption seen in aseptic loosening (see discussion).

Merck and Co. teach the addition of further bisphosphonates to the cement, added to the polymeric base (page 9, lines 18-19). The bisphosphonate applicable in the cement includes the free acids and pharmaceutically acceptable salts and barium salts of alendronate, clodronate, tiludronate, YM 175, ibandronate, risedronate, piridronate, pamidronate or combinations thereof (see page 5). Inhibition of bone resorption is used to refer to bone loss, especially the inhibition of removal of existing bone either from the mineral phase and/or the organic matrix phase, through direct or indirect alteration of osteoclast formation or activity (see page 6). The term "cement" encompasses the mixed cement composition containing all the ingredients and components prior to, during and after complete curing (see page 7). The PMMA beads have a substantially uniform particle size of about 5 to 20 microns average diameter (page 7 last paragraph). The polymer powder part can also contain a radiopaquing agent e.g. barium sulfate (page 8, 2nd paragraph). The amount of bisphosphonate is generally from 0.005 to 10 percent of the total cement composition.

It would have been obvious to one of ordinary skill in art at the time it was made to add additional bisphosphonates as cited in Merck and Co. Such a modification would have been motivated by the reasoned expectation of producing a bone

cement/bisphosphonate composition, which is effective in comprehensively preventing formation of osteoclasts, and loosening of prosthetic implants.

Regarding applicant's remarks that when the particle size of the cement is about the same as the particle-size distribution of the anti-resorptive agent surprisingly prevents clumping and promotes even distribution of the anti-resorptive agent in the composition, Remington's Pharmaceutical Sciences, teaches that, in mixing powders, a large difference in particle size would tend to cause demixing (page 1570 1st full paragraph). Thus, when the particle sizes are similar, the powders would tend to stay mixed. It would have been made obvious to one of ordinary skill in art at the time it was made to employ similar particle sizes of different agents motivated by the teaching of Remington's Pharmaceutical Sciences that a large difference in particle size would tend to cause demixing of a composition of powders.

Please note that applicant's claims are directed to a composition. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re

Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product). In this case, the fact that the anti-resorptive agent is added to the polymeric component does not change the fact that the end product in both the prior art and the instant application are both a bone cement with anti-resorptive agent added. If applicant wants to claim the process of mixing, the patentability analysis would be different for "method of making" claims.

Response to Arguments

Regarding declaration, the statements failed in their purpose since they recited conclusions or opinions with no facts to support or buttress these conclusions. Applicant states that Sabokbar et al. and Merck Co. do not teach or suggest a bone cement composition wherein an antiresorptive agent is present in an amount that does not compromise the bone cement's chemical or mechanical properties as claimed herein. The comparison of the bone cement instantly claimed (MSKCC shown in fig. 1) is compared to bone cement without any addition of anti resorptive agents and to

"MERCK" wherein 90 mg of pamidronate is mixed with 40 g of Simplex. This would be a 0.225% mixture of bisphosphonate in the bone cement. The Merck reference teaches the amount of bisphosphonate is generally from 0.005 to 10 percent of the total cement composition. Thus, the comparison is for one aspect of the Merck reference, but not for every embodiment. Further, the Declaration refers only to the system described in the above referenced application and not to the individual claims of the application. Thus, there is no showing that the objective evidence of nonobviousness is commensurate in scope with the claims. See MPEP § 716. In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe
Patent Examiner
Art Unit 1614

January 7, 2008